REMARKS

Amendments to the Claims

Applicants herein cancel claims 25-26 and 63-75 without prejudice or disclaimer, such that claims 33-62 are now pending. Applicants respectfully request the entry of the amendments.

Claims 33-62 Are Definite Under 35 U.S.C. § 112, Second Paragraph

The Office raises several new grounds of rejection in this Office Action. The Office continues to reject the claims under 35 U.S.C. § 112, Second Paragraph, asserting that there is no antecedent basis for the phrase "the protease activating blood clotting factor VII" in claims 33 and 48. (Office Action at page 3.)

Applicants again traverse that rejection.

The M.P.E.P. counsels examiners that claims that are otherwise clear to one of ordinary skill in the art within the context of the application as a whole should not be rejected merely because they might have been phrased differently. M.P.E.P. § 2173.02. Therefore, there is no *per se* rule that, merely because the word "the" is used to introduce a claim element in its first instance, that claim element must always be indefinite.

Instead, the standard for definiteness according to M.P.E.P. § 2173.02 is one of ***reasonableness***, not absolute precision. That standard is based upon how one of ordinary skill in the art, who has read the specification in full and who is aware of the related art, would understand the claims. M.P.E.P. § 2173.02; *and see Phillips v. AWH*, 415 F.3d 1303 (Fed. Cir. 2005) (*en banc*) (explaining that claims are interpreted in light of the specification as a whole).

It is clear from the application as a whole that "the protease activating blood clotting factor VII" is the name of the protein that is the subject of this application. The fact that the name starts with the word "the" does not make the claims indefinite, especially as that phrase is used in the title and repeatedly throughout the application. (*See, e.g.,* the Title, first full paragraph at page 1, second paragraph at page 1, first full paragraph at page 3, and original claim 1.)

As the M.P.E.P. further makes clear, patent applicants are allowed to be their own lexicographers. *See* M.P.E.P. § 2173. Thus, a patent applicant should not be penalized for choosing to use a name for a claimed protein that begins with the word "the" as opposed to some other name. Moreover, while theoretically, merely to speed prosecution, the claims could be amended to either entirely remove the word "the" from the name or to recite the word "a" instead of "the," Applicants submit that the resulting claim language would be awkward and would not follow correct English grammar and style.

Because the claims as presently drafted are already definite, Applicants submit that there is no reason to amend the claims in a way that does not follow proper English grammar and style. Hence, Applicants request the withdrawal of this rejection.

As an aside, Applicants also note that the Office (via the present Examiner) has already issued at least two United States patents containing the same phrases that are now being rejected here. Those patents are Nos. 6,573,056 and 6,670,455, the latter of which is the parent of the instant application. Applicants again urge the Office to maintain a consistent policy when examining the claim language in these cases.

Claims 33-62 are Supported by the Application as a Whole, under 35 U.S.C. § 112, First Paragraph

The Office continues to assert that the pending claims are not sufficiently supported by the application as a whole because the claims allegedly recite only partial sequences rather than complete sequences for those proteins. (Office Action at pages 3-6.) Applicants traverse this rejection. As explained in detail below, this rejection does not follow the legal standards set by the Federal Circuit, which the Office must apply.

Written description support is judged from the standpoint of one of ordinary skill in the art. M.P.E.P. § 2163. The standard for written description is whether one of ordinary skill in the art would reasonably conclude from reading the application as a whole and from access to the prior art that the applicant had possession of the claimed invention. *See* M.P.E.P. § 2163(I).

Under that standard, "there is no *per se* rule that an adequate written description of an invention that involves a biological macromolecule must contain a recitation of known structure." *Falkner v. Inglis*, 448 F.3d 1357, 1366-1367 (Fed. Cir. 2006). The Federal Circuit has made that point clear several times in overruling written description rejections made by the Office or lower courts where claims to proteins or nucleic acid molecules. *Capon v. Eshhar*, 418 F.3d 1349, 1360-61 (Fed. Cir. 2005); *Invitrogen Corp. v. Clonetech Labs., Inc.*, 429 F.3d 1052, (Fed. Cir. 2005); *Falkner v. Inglis*, 448 F.3d at 1367-68 (Fed. Cir. 2006). All three of those cases dealt with claims drawn to proteins or nucleic acid molecules that did not recite sequence information. In addition, the specifications of the patents at issue did not recite complete sequences for all of the claimed material. However, it was clear to the Federal Circuit in all three instances that the patent applicants possessed the claimed proteins or nucleic acids because skilled

artisans could have found sufficient information to obtain the claimed molecules from the general guidance provided in the applications and from the scientific literature.

The Court particularly emphasized in *Falkner* that "*Eli Lilly* does ***not*** set forth a *per se* rule that whenever a claim limitation is directed to a macromolecular sequence, the specification must always recite the gene or sequence, regardless of whether it is known in the prior art." *Falkner v. Inglis*, 448 F.3d at 1367 (Emphasis in original). Instead, the level of support evolves as the knowledge pertaining to each field of research evolves. *Falkner*, 448 F.3d at 1368. Accordingly, the Court's holding was that "where . . . accessible literature sources clearly provided, as of the relevant date, genes and their nucleotide sequences (here "essential genes"), satisfaction of the written description requirement does not require either the recitation or incorporation by reference (where permitted) of such genes and sequences." *Id.*

Once again, what the Court explained in *Falkner* was that where the literature provides any necessary sequence information, there is no need to recite the information again in either the specification or the claims to meet the written description requirement. In this case too, the literature provides the sequence information for the claimed protease and its proenzyme. Thus, no more is needed.

But here, Applicants have provided even more guidance than was held acceptable in the *Falkner* case. Applicants here have specifically directed one of ordinary skill in the art to two publications that together provide partial and complete amino acid and gene sequences of the claimed protease and its proenzyme. And Applicants have even, merely for the sake of advancing prosecution, provided partial sequences of the protein in the claims. (See the bottom of page 1 of the specification

and claims 33 and 48.) In addition, some of the biological activities of the protease are also summarized in the *Annals of Hematology*, Vol. 78 abstract, by J. Roemisch et al., which was submitted to the Office on September 7, 2006.

A written description rejection similar to the one the Office makes here was also overruled by the Federal Circuit court in *Capon v. Esshar, supra*, and the matter was remanded to the Office. The claims at issue in that case were drawn to chimeric protein constructs made by attaching an antibody fragment to another protein segment. The claims recited no sequence information, but referred to the names of the proteins in the chimera.

In overruling the Office's written description rejection, the Court explained that "[t]he 'written description' requirement must be applied in the context of the particular invention and the state of the knowledge. The Board's rule that the nucleotide sequences of the chimeric genes must be fully presented, although the nucleotide sequences of the component DNA are known, is an inappropriate generalization. When the prior art includes the nucleotide information, precedent does not set a *per se* rule that the information must be determined afresh." 418 F.3d at 1358.

The Court went on to add that "[t]he chimeric genes here at issue are prepared from known DNA sequences of known function. The Board's requirement that these sequences must be analyzed and reported in the specification does not add descriptive substance. The Board erred in holding that the specifications do not meet the written description requirement because they do not reiterate the structure or formula or chemical name for the nucleotide sequences of the claimed chimeric genes." *Id.*

As in *Capon v. Esshar*, the Office here has overlooked: (1) that the protease activating blood clotting factor VII was a known protein when this application was filed, (2) that the gene and amino acid sequences of the protease activating blood clotting factor VII and its proenzyme had already been published, and (3) that the application itself points those of ordinary skill to the article that provides those sequences. Moreover, the application points to an earlier German patent application that provides further information about the sequence of the protein and its biological function and activities. As in *Capon v. Esshar*, adding the sequence to the instant application or claims would be wasteful and unnecessary.

As the case law cited above also clarifies, there is no per se rule that a complete sequence is necessary to satisfy the written description requirement. Thus, even if all that was known were partial sequences and a biological activity, such as the activation of factor VII, there is no reason that this information should be insufficient for claims drawn to the protein that may be extracted from biological fluids. For example, the partial sequences may be used to confirm the identity of bands of protein obtained, as may functional tests.

For all of the above reasons, no additional information is needed to show that Applicants were in possession of the instant compositions, and Applicants request the withdrawal of this rejection so that prosecution may be advanced.

Claims 33-62 are Enabled Under 35 U.S.C. § 112, First Paragraph

Next, the Office continues to reject the pending claims, asserting that they are not enabled throughout their full scope. (Office Action at pages 6-15.) The Office also

bases that assertion on the fact that the claims do not include the full sequence of the claimed protease and proenzyme. (See the Office Action at pages 6-7.)

Applicants also continue to traverse that rejection.

As Applicants have explained above, the instant application refers to German Application No. 19 903 693.4 for and to the 1996 Choi-Miura article, cited below, for the complete sequence of the protease and for the identification and further information regarding the proenzyme and its protease, its biological functions and activities, and how it may be obtained from plasma samples. (*See* the Specification at page 1, second paragraph.) Hence, for reasons given in the preceding section, there is no need to recite the complete sequence of the protease in the claims in order to satisfy the requirements of 35 U.S.C. § 112. Section 2164.01 of the M.P.E.P. also explains that information known in the art need not be repeated in the application text in order to satisfy the enablement requirement.

Moreover, the instant application describes specific methods of purifying the proenzyme and the protease. The Office considers such methods to be enabled, as parent patent 6,670,455 B1, previously examined by the instant Examiner, claims such methods. The application also devotes considerable discussion to methods of obtaining that particular proenzyme and its protease from blood plasma samples. (*See* the working examples.) In addition, to help one of ordinary skill to verify that he has purified the correct protein, the instant application and the prior art to which the Applicants direct one of ordinary skill provide partial and complete sequences. (See the Specification at page 1, second paragraph.) The application also explains that the instant protease activates factor VII, serving as the basis for a simple activity test following purification of

the protease. Moreover, the German patent application cited at page 1 of the instant specification, and other publications in the prior art provide methods of testing the activity of the claimed protease and proenzyme. Given the state of the art and the level of guidance provided in the application, there is no need for further information to satisfy the enablement requirement.

As to the Office's comments regarding a composition that comprises a mixture of the protease and proenzyme (see claims 48-62; Office Action at pages 8-12), the instant specification teaches methods for purifying the proenzyme, for example. (See Examples 1 and 2.) Page 6 of the application explains that the proenzyme remains intact by carrying out the exemplified methods at acidic pH. It follows from this, that exposing the purified proenzyme to a higher pH would gradually allow for self-cleavage to increasing degrees and that re-exposing the purified proenzyme to low pH would re-stabilize the proenzyme form. Alternatively, once the pure form of the proenzyme is obtained, a portion of the proenzyme sample can be allowed to self-cleave, and then the cleaved and uncleaved portions can be mixed together at low pH or other conditions that prevent self-cleavage, thus creating a mixture of the pure form of the proenzyme and cleaved protease. Accordingly, the specification provides more than adequate guidance on preparing the formulations of claims 48-62.

For the reasons above, the claims are enabled and Applicants continue to request the withdrawal of the enablement rejection.

Claims 33, 39, and 45-57 Are Novel according to 35 U.S.C. § 102(b)

The Office now contends that claims 33, 39, and 45-57 are anticipated by the Choi-Miura article referred to at the bottom of page one of the application text. (Office

Action at pages 15-16) (*J. Biochem.* 119: 1157-1165 (1996); "Choi-Miura.") Applicants traverse that rejection because, while Choi-Miura does provide the protease and proenzyme sequences, as previously described, Choi-Miura does not teach a pure form of a proenzyme for the protease as required by all of the rejected claims.

Indeed, as Applicants previously explained, Choi-Miura does not describe the purification of any particular form of the protein. Examining Figure 1 of Choi-Miura, at page 1159, for example, it appears that Choi-Miura and co-authors simply extracted the protein from blood plasma in ***two or more bands***. This indicates that what they obtained was a mixture of at least two different forms or fragments of the protein.

In addition, page 1159, Figure 1(b), of the article depicts the N-terminal sequences of the 50 kDa and 17 kDa bands of the protein that Choi-Miura and co-authors obtained. If Choi-Miura had extracted a proenzyme, at least one of those N-terminal sequences would contain proenzyme sequence. But they do not. Instead, the bands Choi-Miura obtained all start from within the sequence of the protease, indicating that Choi-Miura obtained only protease or its fragments.

Specifically, the sequence called "Sequence 1" starts at the beginning of the protease sequence, as can be seen by comparing that sequence to the sequence of the proenzyme presented in Figure 6. "Sequence 2" starts even further downstream. If, instead, Choi-Miura had purified a proenzyme, the N-terminal sequences would have included portions of the leader sequence shown in Figure 6 of the paper. The Sequences 1 and 2 from the N-terminal of the smaller, 17 kDa band also come from inside the protease sequence, again indicating that this fragment is not a pure proenzyme but a portion of the cleaved protease.

While Choi-Miura's Figure 6 does provide a gene and amino acid sequence for the proenzyme and shows the site of cleavage, that sequence was obtained by analyzing the gene sequence and not by purifying a proenzyme.

Thus, Choi-Miura does not teach all of the elements of the claims and the Office has not established a *prima facie* case of anticipation on the basis of this article. Hence, Applicants request the withdrawal of this rejection.

Claims 33-62 Are Nonobvious according to 35 U.S.C. § 103

Finally, the Office rejects claims 33-36, 38-39, and 43-47 as allegedly obvious over Choi-Miura et al. (*J. Biochem.* 119: 1157-1165 (1996); "Choi-Miura") in combination with Turner et al. (U.S. Patent No. 5,326,558; "Turner"). (Office Action at pages 13-15.) Applicants continue to traverse this rejection.

An evaluation of obviousness involves:

(A) Determining the scope and contents of the prior art;

(B) Ascertaining the differences between the prior art and the claims in issue;

(C) Resolving the level of ordinary skill in the pertinent art; and

(D) Evaluating evidence of secondary considerations.

See M.P.E.P. § 2141; *Graham v. John Deere Co.*, 383 U.S. 1 (1966).

Choi-Miura and Turner, taken together, do not teach or suggest how to obtain either a pure proenzyme of claim 33. Accordingly, the also do not teach or suggest how to obtain a mixture of those pure forms as claimed in claim 48.

The Office again cites Turner only for discussion of protease inhibitors, recited in some of the claims. (Office Action at page 14.) Turner does not pertain to the instant protease or proenzyme or suggest the other elements of claims 33-62. Thus, Turner is

of no relevance when considering what the prior art teaches about how to obtain a pure form of a protease for the proenzyme activating blood clotting factor VII.

Choi-Miura does not teach or suggest how to predictably obtain a pure form of the protease or a pure form of the proenzyme. Indeed, as described above, Choi-Miura and co-workers were unable to obtain a proenzyme species and instead only obtained a mixture of full length protease with protease fragments. (See section above.)

It is only Applicants who have devised a preparatory scheme that specifically purifies the proenzyme and who have determined which conditions may be used to prevent self-cleavage during the preparation. To purify the proenzyme, for example, Applicants identified conditions, such as a pH range that de-activates contaminating plasma proteases, thus preventing the proenzyme from being cut apart during the purification process. (See the application at page 6.) Applicants discovered, for instance, that modifying conditions such as pH helped to avoid unwanted cleavage of the proenzyme. Moreover, Applicants devised purification protocols such as that of Example 2 that allow for purification of a proenzyme form of the protease. See, for instance, the specification at page 3, last paragraph, to page 5, line 3.

Thus, comparing the teachings of the prior art to the instant claims, it is evident that the combination of Choi-Miura and Turner cannot render any of the pending claims obvious. Accordingly, Applicants request the withdrawal of this rejection.

Conclusion

In view of the foregoing amendments and remarks, Applicants request the withdrawal of all of the instant rejections, and submit that this application is in condition for allowance. Hence, Applicants respectfully request the allowance of all of the subject

matter of claims 33-62 and the re-joiner of any non elected limitations within those claims.

This Reply is accompanied by a Petition for a One-Month Extension of Time and fee payment to extend the response period to December 6, 2007. Please grant any extensions of time required to enter this response and charge any required fees not found herewith to our deposit account 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: December 5, 2007

By: _____
Elizabeth A. Doherty
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Attachment: Petition for One-Month Extension of Time (with fee enclosed)